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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,311	11/09/2001	Natasha V. Raikhel	MSU 4.1-633	4340

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EXAMINER
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ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 07/31/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,311	RAIKHEL ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's election without traverse of Group I in Paper No. 14, filed 12 May 2003, is acknowledged. Applicant's amendments of the claims, the specification, the drawings filed 12 May 2003 have been entered. Claims 1 and 3-4 are pending, and will be examined to the extent they read on nucleic acids encoding plant fucosyl transferases.

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (*i.e.*, continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

3. The drawings are objected to. Applicant requested that Figure 4 be renumbered Figure 1. However, the Office cannot amend drawings. Applicant must submit a new Figure showing the plasmid map and numbered Figure 1. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

4. The disclosure is objected to because it refers to the following cancelled Figures and Tables:

a. Pg 10, line 27, refers to Figure 1 as showing two proteins co-purifying with XG FTase activity. However, Applicant wishes figure 1 to show a plasmid.

b. Pg 11, line 15, refers to Table 2, which has been cancelled.

c. Pg 11, line 27, refers to Table 3, which has been cancelled.

d. Pg 11, line 29, refers to Table 4, which has been cancelled.

e. Pg 11, line 33, refers to Table 5, which has been cancelled.

f. Pg 14, lines 25-26, refers to Tables 6-14.

Appropriate correction is required.

5. The amendment filed 12 May 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment to the paragraph starting on pg 12, line 10 is objected to for inclusion of the sentence "Anti-ATFT1 polyclonal ... but not pea."

Applicant is required to cancel the new matter in the reply to this Office Action.

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from pg 14, lines 8 and 10.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

Claim Objections

7. Claim 3 is objected to because of the following informality: "comprising" in line 2 should be replaced with "wherein the method comprises".

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to plant fucosyl transferase genes and gene products, which are products of nature.

Claim 1, as written, does not sufficiently distinguish over nucleic acids and proteins as they exist in nature because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that the claim be modified to refer to the hand of the inventor, *e.g.* by indicting the items are isolated or purified. See MPEP 2105.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding SEQ ID NO:1, does not reasonably provide enablement for nucleic acids encoding any plant fucosyltransferase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claim is broadly drawn to any nucleic acid that encodes any fucosyltransferase from any plant.

The instant specification, however, only provides guidance for purification of a xyloglucan fucosyltransferase (FTase) from pea (pg 8-9), assay of FTase activity (pg 9-10), sequencing of the FTase (pg 10-11) and the use of the peptide sequences to identify Arabidopsis ESTs that encode proteins with homology to the peptides and use of the sequences to isolate a full-length cDNA (SEQ ID NO:2, which encodedes SEQ ID NIO:2) (pg 11-12), preparation of antibodies to the Arabidopsis FTase, immunoprecipitation of the protein and confirmation that it encodes an FTase (pg 12-13), expression of the gene in COS cells (pg 13) and general guidance for plant transformation (pg 16-18).

The instant specification fails to provide guidance for a nucleic acid that encodes any fucosyltransferase from any plant. The instant specification fails to provide guidance for exact hybridization or amplification conditions and probes/primers to use in isolation of nucleic acids other than SEQ ID NO:2.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO:1 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain FTase activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

The instant specification fails to teach the critical amino acids of fucosyltransferases. The art at the time of filing and even after the time of filing teaches that the critical amino acids of plant fucosyltransferases cannot be predicted. Faik et al (2000, J. Biol. Chem. 275:15082-15089) teach that more studies using site-directed mutagenesis is required to determine the locations of the residues of the catalytically essential amino acids of the pea xyloglucan fucosyltransferase (pg 15085, right column, 1st paragraph). Leiter et al (1999, J. Biol. Chem. 274:21830-21839) teach that only one region of the mung bean GSP-L-Fuc:Asn-linked GlcNAc α1,3-fucosyltransferase showed significant homology to animal and bacterial α1,3/4-fucosyltransferases; however, it has a different amino acid sequence in the region thought to be involved in the catalytic site and has no obvious sequence similarity with mammalian α1,6-fucosyltransferases despite sharing substrate specificity (pg 21838, paragraph spanning the columns).

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of

those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have at least 95% identity to the original protein. The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

12. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is broadly drawn to any nucleic acid that encodes any fucosyltransferase from any plant. In contrast, the specification only describes a coding sequence from Arabidopsis that comprises SEQ ID NO:2. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

The claim fails to recite a specific fucosyltransferase activity. A variety of fucosyltransferase activities are known, including α1,2-fucosyltransferases, α1,3/4-fucosyltransferases and α1,6-fucosyltransferases (Staudacher et al, 1999, Biochim. Biophys. Acta 1473:216-236; see pg 220-221 and pg 225). In plants there appear to be more than one xyloglucan fucosyltransferase, as the structure of xyloglucan differs among species; for example, sycamore has either two such enzymes or a single enzyme with unique enzymatic

properties (Faik et al, *supra*; see pg 15082, right column, paragraph 1, and pg 15088, right column, paragraph 2).

Hence, Applicant has not, in fact, described DNA molecules that encode a fucosyltransferases within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 1 is in improper form for claiming more than one product.

Claim 1 is indefinite in its recitation of "gene products". It is not clear what is intended. RNA? Protein? Both?

Claim 4 lacks antecedent basis for the limitation "the transformed cell of claim 3" as claim 3 is drawn to a method.

15. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The method is one of producing a transformed plant expressing fucosyltransferase. However, the only method step is that of transforming a plant cell. The omitted steps are those involving regenerating a plant from the plant cell and those ensuring that the plant expressed fucosyltransferase.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Newman et al (1994, GenBank Accession No. R90192).

Newman et al teach a nucleic acid from *Arabidopsis* with 97.4% similarity to a nucleic acid that encodes SEQ ID NO:1. This nucleic acid would thus encode a plant fucosyltransferase and would thus be a plant fucosyltransferase gene.

18. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Rounsley et al (1998, EMBL Accession No. T02704).

Rounsley et al teach a nucleic acid from *Arabidopsis* that encodes a protein with 100% identity SEQ ID NO:1. This nucleic acid would thus be a plant fucosyltransferase gene.

19. Claims 3-4 are free of the prior art, given the failure of the prior art to teach or suggest the transformation of a plant with a gene encoding a xyloglucan fucosyltransferase, including that of SEQ ID NO:1.

Conclusion

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
July 30, 2003